REMARKS

Claims 21-27 and 29-38 are pending in the application. All pending claims are rejected under 35 USC § 103(a) as being obvious over Petre *et al.* (WO 93/24148) in view of Arminjon *et al.* (AU 708777 or WO 96/37222). For the following reasons, the Applicant respectfully traverses.

The Office Action first sought to refute that applicants argument that the prior art does not teach adsorption of tetanus and diphtheria toxoids onto an aluminum salt prior to mixing with the other components.

As suggested by its title ("Combined Vaccines Comprising Hepatitis B Surface Antigen and Other Antigens"), Petre *et al.* is concerned with making HBsAg-containing vaccine compositions with increased stability/immunogenicity of the HBsAg component relative to the prior art. There is no suggestion in Petre *et al.* that its teachings are generally desirable outside this setting.

The Office Action points to a passage on page 9, ll. 1-3, which states, "After allowing time for complete and stable adsorption of the respective components, the different components are combined under appropriate conditions." Based upon this, the Examiner concludes, that Petre *et al.* "clearly teaches adsorption prior to mixing with other components."

But the sentence relied upon is taken out of context. The full paragraph containing this sentence states:

> The required DT, DTPw, DTPa, HA or other components are adsorbed onto a suitable adjuvant, especially AH or AP; HBsAg is absorbed onto a suitable stabilizing adjuvant, selected as hereinabove described, especially an aluminum salt other than AH. Preferably it is adsorbed onto AP. After allowing time for complete and stable adsorption of the respective components, the different components are combined under appropriate conditions.

Petre *et al.*, p. 8, l. 36 through p. 9, l. 3. Viewed in context it is clear that Petre *et al.* is teaching that in making a composition comprising HBsAg and other components, HBsAg is adsorbed onto a suitable adjuvant separately from and before being mixed with the other components. That is, Petre *et al.* teaches that whatever the non-HBsAg components are, they are to be adsorbed on a suitable adjuvant separately from HBsAg. Petre *et al.* does not teach or suggest that diphtheria toxoid and tetanus toxoid in particular (as opposed to any other components) should be pre-adsorbed onto an aluminum salt before being mixed with other components. Nor does Petre *et al.* teach or suggest

that diphtheria toxoid and tetanus toxoid should be pre-adsorbed onto an aluminum salt in a context other than in preparing an HBsAg-containing vaccine composition.

Furthermore, the above-quoted statement by Petre *et al.* that the non-HBsAg components are adsorbed onto a suitable adjuvant before being mixed with HBsAg is, in fact, ~~a teaching away~~ from presently pending claims such as 23, which states that the inactivated polio virus component is mixed with other components without be adsorbed onto an aluminum salt.

In addition, in response to the Applicants' previous assertion that the Office Actions had failed to identify each of the limitations of the claims, the Examiner asserted that Petre *et al.* discloses instances where only one of the components of the multivalent vaccine is adsorbed to an aluminum salt. This statement further undercuts the basis for this rejection as it demonstrates that Petre *et al.* in fact does not suggest pre-adsorbing both diphtheria toxoid and tetanus toxoid on a suitable adjuvant since it teaches that one can equally well pre-adsorb only a single non-HBsAg antigen before mixing it with non-HBsAg.

The Office Action next alleged that Arminjon *et al.* teaches that PRP-T should be prepared in a buffer solution before mixing, referring to Arminjon *et al.* p. 6, ll. 33-40. But a careful reading of this passage reveals that it is merely concerned with whether anions (*e.g.*, citrate ions and phosphate ions) should be added to aluminum complexes (*i.e.*, aluminum salt adjuvants such as aluminum phosphate and aluminum hydroxide) before or after PRP-T has been added. That is, this passage is concerned with the order of adding PRP-T to an aluminum complex with respect to the addition of anions, **not** with respect to the addition of other antigens (as presently claimed). Arminjon *et al.* contains no teachings or suggestion vis-à-vis the order mixing PRP-T with the other antigens

The Office Action also alleges that it would have been obvious to combine Arminjon *et al.* with Petre *et al.* because Arminjon teaches that the method of Petre *et al.* is inefficient, the Office Action referring to Arminjon *et al.* p. 2, ll. 20-26, for support. But Arminjon *et al.* p. 2, ll. 17-26, states:

> In fact, the solution proposed in the prior art and consisting in a special syringe with two compartments (a first compartment containing the PRP-T in lyophilized form and a second compartment containing the other antigens in aqueous suspension) whose contents are mixed for use only at the time of administration is not satisfactory either at the level of the costs of production or at the level of the operations to e carried out by the practitioner.

Petre *et al.*, however, contains no such teachings referred to by Arminjon *et al.* of the use of a dual compartment syringe containing PRP-T in lyophilized form in one barrel and the remaining antigens in

aqueous suspension in the second. Thus, whatever prior art Arminjon *et al.* is referring to in this passage, it is not Petre *et al.* As noted above, Petre *et al.* is merely concerned with the preparation of HBsAg compositions made by adsorbing HBsAg on an adjuvant separately from other components. Thus, the Applicants respectfully submit that the alleged suggestion for combining Petre *et al.* and Arminjon *et al.* is false and that there is simply no such suggestion in the cited art.

Lastly, in response to the Applicants' previous assertion that the Office Actions had failed to identify each of the limitations of the claims, the Office Action (a) invited the applicants to review the prior Office Actions and (b) stated that whereas present claim 23 recites a composition in which inactivated polio virus is not adsorbed onto an aluminum salt, Petre *et al.* teach instances in which only a single component of the multivalent vaccine is adsorbed on aluminum salt. With regard to (a), the applicants have carefully reviewed all the Office Actions and are unable to locate anywhere that identifies in the prior art (1) each and every element of each and every claim under rejection, (2) the suggestion to combine each and every element of each and every claim under rejection as recited in the claims, and (3) a reasonable expectation of success (in particular that the claimed compositions would not suffer from antigenic interference). Without such allegations, a *prima facie* case of obviousness has not been made.

With regard to (b), the applicants respectfully submit that the teaching of Petre *et al.* that only a single non-HBsAg antigen need be adsorbed on an aluminum salt is contrary to the present claims, which recite that both tetanus toxoid and diphtheria toxoid are adsorbed onto the aluminum salt before being mixed with the other components. The limitation of claim 23 referred to by the Examiner is merely one of a number of limitations found throughout the claims. Furthermore, claim 23 depends from claim 21, which recites pre-adsorption of both tetanus toxoid and diphtheria toxoid on an aluminum salt before mixing with the other recited components.

In view of the foregoing, therefore, the present claims cannot be obvious. The Applicant respectfully requests reconsideration and withdrawal of this rejection.

The Patent Office is invited to contact the undersigned representative if it is believed that this would be helpful in expediting prosecution of this application. The Applicant submits that the pending claims are in condition for allowance, and issuance of a Notice of Allowance is respectfully requested.

If there are any questions or comments regarding this Response or application, the Examiner is encouraged to contact the undersigned attorney as indicated below.

Respectfully submitted,

Date: June 6, 2003

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